

REMARKS

Claims 130-162 were pending the application. Claims 130 and 131 have been amended. Upon entry of this amendment, claims 130-162 will remain pending. For the Examiner's convenience the currently pending claims are set forth in Appendix A.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendments. The attached page is captioned "Version With Markings to Show Changes Made."

Support for claim amendments may be found throughout the specification, including the originally filed claims.

Applicants respectfully submit herewith, as Appendices A and B, copies of search queries using the terms, for example, matrix metalloproteinase, MMP, diagnosis or diagnose, cancer, metalloproteinase-associated cancer, MMP-associated cancer, and urine. Applicants utilized the Medline database to search scientific publications and submit herewith, as Appendix A, a copy of the search results, including a list of the nine most relevant citations, which post-date Applicant's priority date. Applicants further submit herewith a Form 1449 citing the nine citations from the Medline search results. Applicants also utilized the Delphion database to search U.S. and European granted patents, as well as U.S., PCT, and European published patent applications, and submit herewith a copy of one patent. A copy of the search results from the Delphion database, including the patent publication or issued patent number, title, abstract, publication date, filing date, and priority date, are submitted herewith as Appendix B. Applicants respectfully note that the term urine significantly narrowed the search results. Applicants further note that publications and patent applications by the inventors of the present invention were identified in the aforementioned searches.

No new matter has been added. Any amendments to and/or cancellation of the claims was done solely for the purpose of expediting prosecution of the present

application. Applicant reserves the right to pursue the subject matter of the claims as originally filed in this or a separate application(s).

Acknowledgement of Telephonic Interview with the Examiner

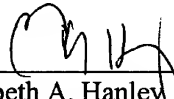
Applicants gratefully acknowledge the telephonic interview with the Examiner regarding the present application.

CONCLUSION

In view of the foregoing amendments and foregoing remarks, it is respectfully submitted that the application is in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' Attorney at (617) 227-7400.

Respectfully submitted

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Date: June 13, 2003

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Please amend claims 130 and 131 as follows:

130. **(Amended)** A non-invasive method for facilitating the diagnosis of a subject for a matrix metalloproteinase –associated (MMP-associated)) cancer, comprising:

obtaining a urine sample from a subject;

detecting the presence or absence of a matrix metalloproteinase in the urine sample; and

correlating the presence or absence of the matrix metalloproteinase in the urine sample with the presence or absence of the MMP-associated cancer, thereby facilitating the diagnosis of the subject for the MMP-associated cancer.

131. **(Amended)** A non-invasive method using at least one biological marker to monitor the prognosis or diagnosis of a subject for a matrix metalloproteinase –associated (MMP-associated) cancer, comprising:

obtaining a urine sample from a subject; and

monitoring the prognosis or diagnosis of the subject for an MMP-associated cancer using at least one biological marker including a matrix metalloproteinase in the urine sample selected for its association with the cancer.

APPENDIX A: PENDING CLAIMS

130. **(Amended)** A non-invasive method for facilitating the diagnosis of a subject for a matrix metalloproteinase –associated (MMP-associated)) cancer, comprising:

obtaining a urine sample from a subject;
detecting the presence or absence of a matrix metalloproteinase in the urine sample; and
correlating the presence or absence of the matrix metalloproteinase in the urine sample with the presence or absence of the MMP-associated cancer, thereby facilitating the diagnosis of the subject for the MMP-associated cancer.

131. **(Amended)** A non-invasive method using at least one biological marker to monitor the prognosis or diagnosis of a subject for a matrix metalloproteinase –associated (MMP-associated) cancer, comprising:

obtaining a urine sample from a subject; and
monitoring the prognosis or diagnosis of the subject for an MMP-associated cancer using at least one biological marker including a matrix metalloproteinase in the urine sample selected for its association with the cancer.

132. The method of claim 130 or 131, wherein the MMP-associated cancer is organ-confined prostate cancer.

133. The method of claim 130 or 131, wherein the MMP-associated cancer is metastatic prostate cancer.

134. The method of claim 130 or 131, wherein the MMP-associated cancer is in cells of epithelial origin.

135. The method of claim 130 or 131, wherein the MMP-associated cancer appears in cells of mesodermal origin.

136. The method of claim 130 or 131, wherein the MMP-associated cancer appears in cells of endodermal origin.

137. The method of claim 130 or 131, wherein the MMP-associated cancer affects cells of bone or of hematopoietic origin.

138. The method of claim 130 or 131, wherein the MMP-associated cancer is a cancer of the nervous system.

139. The method of claim 130 or 131, wherein the MMP-associated cancer is a breast cancer.

140. The method of claim 130 or 131, wherein the MMP-associated cancer is a retina cancer.

141. The method of claim 130 or 131, wherein the MMP-associated cancer is a lung cancer.

142. The method of claim 130 or 131, wherein the MMP-associated cancer is a skin cancer.

143. The method of claim 130 or 131, wherein the MMP-associated cancer is a kidney cancer.

144. The method of claim 130 or 131, wherein the MMP-associated cancer is a liver cancer.

145. The method of claim 130 or 131, wherein the MMP-associated cancer is a pancreatic cancer.

146. The method of claim 130 or 131, wherein the MMP-associated cancer is a cancer of the genito-urinary or gastrointestinal tract.

147. The method of claim 130 or 131, wherein the MMP-associated cancer is bladder cancer.

148. The method of claim 130 or 131, wherein the MMP-associated cancer is a lymphoma.

149. The method of claim 130 or 131, wherein the matrix metalloproteinase is a proenzyme.

150. The method of claim 130 or 131, further comprising removal of low molecular weight contaminants from the urine prior to the detection step.

151. The method of claim 130 or 131, wherein the urine is dialyzed.
152. The method of claim 130 or 131, wherein the subject has previously been treated surgically or hormonally.
153. The method of claim 130 or 131, wherein the subject has been treated to block testosterone.
154. The method of claim 130 or 131, wherein the matrix metalloproteinase is a gelatinase.
155. The method of claim 130 or 131, wherein the matrix metalloproteinase has a molecular weight of approximately 72 kDa.
156. The method of claim 130 or 131, wherein the matrix metalloproteinase has a molecular weight of approximately 92 kDa.
157. The method of claim 130 or 131, wherein the matrix metalloproteinase has a molecular weight of approximately 150 kDa.
158. The method of claim 130 or 131, wherein the matrix metalloproteinase is detected or monitored electrophoretically.
159. The method of claim 158, wherein the electrophoretic pattern is a zymogram.

160. The method of claim 130 or 131, wherein the matrix metalloproteinase is detected or monitored immunochemically.

161. The method of claim 160, wherein matrix metalloproteinase is detected or monitored by a radio-immune assay.

162. The method of claim 160, wherein the matrix metalloproteinase is detected or monitored by an enzyme-linked immunosorbant assay.